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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,935	02/25/2004	Albert J. Robichaud	PH7218A CIP	5060

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STEPHEN B. DAVIS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER	
KIFLE, BRUCK	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 07/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,935	ROBICHAUD ET AL.	
	Examiner	Art Unit	
	Bruck Kifle, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's response filed 06/23/05 have been received and reviewed. Claims 1-34 are still pending in this application.

Claim Rejections - 35 USC § 112

Claims 1-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to treating addictive behavior and sleep disorders. It is unclear which addictive behavior and sleep disorder is intended and which one is not as these groups include unrelated (addiction to opiates, nicotine, alcohol, etc.) and/or embrace "opposites" (e.g. sleeplessness and narcolepsy). Applicants response is point to the specification to page 3, line 17 to page 4, line 25 and page 4, line 26 to page 5, line 14. These lines have been reproduced below. One skilled in the art cannot say from these lines which sleep disorders are intended and addiction to which substance is intended.

> **Serotonin (5HT) may have a critical role in the regulation of some drug-induced addictive behaviors. Serotonin is involved in neuronal processes related to inhibitory control and impulsivity. (Roy et al., Acta Psychiotr. Scand. 78 (1988) 529-535; Soubrie et al., Behav. Brain. Sci. 9 (1986) 319-364) Some studies have implicated serotonergic mechanisms in the development or expression of drug-induced sensitization (King et al., Psychopharmacology 130 (1997) 159-165; Olausson et al., Psychopharmacology 142 (1999) 111-119) The relationship between 5HT and impulsive behavior as well as drug intake has been described, and manipulations that attenuate 5HT neurotransmission both increase impulsive behavior (Roy et al., Acta Psychiotr. Scand. 78 (1988) 529-535; Soubrie et al., Behav. Brain. Sci. 9 (1986) 319-364) and elevate the intake of various drugs of abuse (Engel et al., in Naranjo, C.A., Sellers, E.M. (Eds.). Novel Pharmacological Interventions for Alcoholism, Springer, New York, pp. 68-82 (1999); Roberts et al., Pharmacol. Biochem. Behav. 49 (1994) 177-182)**
>
> **A series of animal investigations have reported that central 5HT2 receptors are related to the many symptoms associated with drug-dependent withdrawal.**

Withdrawal from chronic exposure to low doses of cocaine causes reversible supersensitivity of 5HT2 receptors in mice. (Baumann et al., Neuropharmacology 35 (1996) 295-301; Darmani et al., Neurotoxicol. Tertol. 22 (2000) 61-69) Moreover, the 5HT2 receptor antagonists, ketanserin and mianserin, block or attenuate morphine withdrawal syndrome in rats. (Neal et al., J. Pharmacol. Exp. Ther. 236 (1986) 157-165; Neal et al., Eur. J. Pharmacol. 132 (1986) 299-304)

The effects of 5HT receptor agonists on the behavioral and neurochemical consequences of repeated nicotine treatment have also been studied. (Olausson et al., Eur. J. Pharmacol. 420 (2001) 45-54) The results of that study provided evidence that repeated daily nicotine treatment is associated with both locomotor sensitization and behavioral disinhibition, and that the expression of those behaviors can be modulated by specific agonists at 5HT receptor subtypes.

Studies with experimental animals have shown that nicotine withdrawal leads to increased sensitivity of serotonergic neurons in the dorsal raphe to 5HT1A agonists in rats. (Rasmussen et al., Psychopharmacology (Berl) 133 (1997) 343-346) Other findings suggest that cessation of chronic nicotine increases the sensitivity to 5HT2 receptor systems, and that the 5HT2 receptor systems may be related to some aspect of the nicotine withdrawal syndrome. (Suemaru et al., Psychopharmacology (Berl) 159 (2001) 31-38) Other studies have also examined the effect of nicotine cessation on the central serotonergic systems in mice and the involvement of 5HT2 receptors. (Yasuda et al., Naunyn-Schmiedeberg's Arch. Pharmacol. 366 (2002) 276-281) The studies by Yasuda et al. suggested that cessation of repeated nicotine administration resulted in increased sensitivity to 5HT2 receptor systems and decreased 5HT2 turnover, and that these phenomena may be related to the manifestation of nicotine withdrawal symptoms.

Modulation of the 5-HT2 receptors has been observed to play a role in sleep disorders. Ritanserin, a selective 5HT2 receptor antagonist, massively enhances slow save sleep (stage 3 and 4) in humans (Declerck et al., Curr. Ther. Res. 41 (1987)427-432; Idzikowsky et al., Psychopharmacology 93 (1987) 416-420; Ikzikowsky et al., Brain Res. 378 (1986) 164-168) and increases deep slow wave sleep in rats. (Detari et al., Psychopharmacology 142 (1999) 318-326; Dugovic et al., Eur. J. Pharmaol. 137 (1987) 145-146; Kantor et al., J. Physiol. 526 (2000) 66-67) Ritanserin and other

5HT2 receptor antagonists increase low frequency EEG activity administered at the beginning of the passive phase of sleep, that is in the light period in rats (Borbely et al., Eur. J. Pharmacol. 156 (1988) 275-278) and in the dark period in humans (Dijk et al., Eur. J. Pharmacol. 171 (1989) 207-218).

The effects of the 5HT2 receptor antagonist ritanserin on electroencephalogram (EEG) power spectra, sleep and motor activity have also been studied. (Kantor et al., Brain Research 943 (2002) 105-111) The studies by Kantor et al. showed that the 5HT2 receptor antagonist ritanserin has longterm effects on EEG power spectra, sleep and motility. Kantor et al. concluded that because ritanserin is a 5HT2 receptor antagonist, under physiological conditions, serotonin increases electroencephalogram (EEG) synchronization and produces an increase in vigilance level and motor activity by tonic activation of 5HT2 receptors. The proposed regulatory mechanism plays an important role in the waking process and the appearances of its effects in the light and dark phases were markedly different.

U.S. Patent Numbers 3,914,421; 4,013,652; 4,115,577; 4,183,936; and 4,238,607 disclose pyridopyrrolobenz-heterocycles of formula:

Claims 1-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating addictive behavior and sleep disorders generally. The basis of this rejection is the same as given in the previous office action and is incorporated herein fully by reference. Applicants response is point to the specification to page 3, line 17 to page 4, line 25 and page 4, line 26 to page 5, line 14 (reproduced above). It was shown

in the previous office action that addictions to different substances require different treatments and that sleep disorders covers "opposites" which cannot be treated by the same drug.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668. The examiner can normally be reached Tuesdays to Fridays between 8:30 AM and 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bruck Kifle, Ph.D.
Primary Examiner
Art Unit 1624

BK
July 21, 2005